

In re Application of: Clarke *et al.*  
Application Serial No.: 09/920,517

196. The enriched population of claim 23, wherein the solid tumor stem cells in the enriched population express the cell surface marker B38.1.

197. The enriched population of claim 23, wherein the solid tumor stem cells in the enriched population express lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor.

198. The method of claim 33, wherein the epithelial cancer is a breast cancer or an ovarian cancer.

### REMARKS

Upon election of the claims of Group I and entry of the present amendments, claims 1-30, 32-40 and 184-198 are pending. Support for the amendments to independent claims 1, 23 and 32 is found in the claims as originally filed and in the specification, *e.g.*, at paragraph 34. Support for the amendments to dependant 2-4, 7-8, 17, 25-26, 37, 39-40 and new claims 184-198 is found in the claims as originally filed. Additional support for new claims 189-193 is found in the specification, paragraphs [17]-[18], [20]-[21], [52], [54], [77], [83], [85], [211] and [228]-[236]. Claims 7 and 15 have been amended to correct typographical errors and to provide consistency. Claim 39 has been amended to correct dependency. Claims 25, 39 and 40 have been amended to provide clarity.

Attached hereto is a marked-up copy of the claims as amended, showing the changes made. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE". No new matter is added.

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (Amended) An isolated solid tumor stem cell, wherein:
  - (a) the solid tumor stem cell is derived from a solid tumor; and
  - (b) ~~the solid tumor stem cell expresses the cell surface marker CD44;~~
  - (e) ~~the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor; and~~
  - (d) the solid tumor stem cell is tumorigenic.
2. (Amended) The isolated solid tumor stem cell of claim 1, ~~further~~ wherein: (e) the solid tumor stem cell expresses the cell surface marker ~~B38.1~~ CD44.
3. (Amended) The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell does not express detectable levels of one or more LINEAGE markers, wherein a LINEAGE marker is selected from the group consisting of CD2, CD3, CD10, CD14, CD16, CD31, CD45, ~~and CD64, and CD140b.~~
4. (Amended) The isolated solid tumor stem cell of claim 3, wherein the solid tumor stem cell does not express detectable levels of LINEAGE markers, wherein the LINEAGE markers comprise CD2, CD3, CD14, CD16, and CD64.
5. (Amended) The isolated solid tumor stem cell of claim 1, ~~further~~ wherein: (e) the solid tumor stem cell expresses the cell surface marker epithelial specific antigen (ESA).
6. The isolated solid tumor stem cell of claim 4, wherein the LINEAGE markers further comprise CD10, CD31, and CD140b.
7. (Amended) The isolated solid tumor stem cell of claim 1, wherein the solid tumor is a sarcoma ~~cell~~ or an epithelial cancer.

8. (Amended) The isolated solid tumor stem cell of claim 7 ~~4~~, wherein the epithelial cancer is a breast cancer or an ovarian cancer.
9. The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell contains a polynucleotide vector.
10. The isolated solid tumor stem cell of claim 9, wherein the polynucleotide vector is a viral vector or a plasmid.
11. The isolated solid tumor stem cell of claim 9, wherein the polynucleotide vector contains a reporter polynucleotide.
12. The isolated solid tumor stem cell of claim 11, wherein the reporter polynucleotide is provides a detectable signal when active in a solid tumor stem cell.
13. The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell further comprises a recombinant polynucleotide.
14. The isolated solid tumor stem cell of claim 13, wherein the recombinant polynucleotide is integrated into a chromosome of the solid tumor stem cell.
15. (Amended) The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell is introduced into a host ~~mammal~~ animal.
16. The isolated solid tumor stem cell of claim 15, wherein the solid tumor stem cell forms a new tumor upon transplantation into the host animal.
17. (Amended) The isolated solid tumor stem cell of claim ~~15~~ 192, wherein the ~~host animal~~ mouse is an immunocompromised mouse.
18. The isolated solid tumor stem cell of claim 1, further comprising a culture medium, in which culture medium the solid tumor stem cell is situated.
19. The isolated solid tumor stem cell of claim 18, wherein the culture medium comprises a Notch ligand.

20. The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell is affixed to a substrate.
21. The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell has been treated to reduce proliferation.
22. The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell has been treated to increase proliferation.
23. (Amended) An enriched population of solid tumor stem cells, wherein:
  - (a) the tumor cells are derived from a solid tumor;
  - (b) ~~the solid tumor stem cell expresses the cell surface marker CD44;~~
  - (e) ~~the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;~~
  - (d) the solid tumor stem cells are is tumorigenic; and
  - (e c) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells.
24. The enriched population of claim 23, wherein the solid tumor is a sarcoma or an epithelial cancer.
25. (Amended) The enriched population of claim 23, wherein the solid tumor stem cells in the enriched population expresses the cell surface marker ~~B38.1~~ CD44.
26. (Amended) The enriched population of claim 23, wherein solid tumor stem cell fails to express at least one ~~lineage~~ LINEAGE marker selected from the group consisting of CD2, CD3, CD10, CD14, CD16, CD31, CD45, ~~and CD64, and CD140b.~~
27. The enriched population of claim 23, wherein the enrichment is in the ability to form new tumors relative to unfractionated tumor cells.
28. The enriched population of claim 23, wherein the population is at least 5-fold enriched.
29. The enriched population of claim 23, wherein the population is at least 10-fold enriched.

30. The enriched population of claim 23, wherein the population is at least 50-fold enriched.
31. (Canceled) A population of cells that have been enriched for non-tumorigenic solid tumor cells, wherein:
- (a) the population is derived from a solid tumor;
  - (b) the population is depleted for the ability to form tumors relative to unfractionated solid tumor cells; and
  - (c) the population is depleted for cells that expresses the cell surface marker CD44 relative to unfractionated solid tumor cells.
32. A method for enriching a population of cells for solid tumor stem cells, comprising the steps of:
- (a) dissociating a solid tumor to form a cell suspension;
  - (b) contacting the dissociated cells with at least one reagent, wherein the reagent either selectively binds to a solid tumor stem cell positive marker or negative marker; and
  - (c) selecting cells that bind to the reagent that selectively binds to a positive marker and/or that do not bind to the reagent that selectively binds to a negative marker, wherein the selected cells are enriched in tumor stem cells as compared with the unfractionated population of solid tumor cells.
33. The method of claim 32, wherein the solid tumor is a sarcoma or epithelial cancer.
34. The method of claim 32, wherein the reagent is an antibody or a lectin.
35. The method of claim 32, wherein the reagent is conjugated to a fluorochrome or to magnetic particles.
36. The method of claim 32, wherein the solid tumor stem cell positive marker is a marker selected from the group consisting of CD44, B38.1 and ESA.
37. (Amended) The method of claim 32, wherein the solid tumor stem cell negative marker is a marker selected from the group consisting of CD2, CD3, CD10, CD14, CD16, CD31, CD45, and CD64, and CD140b.
38. The method of claim 32, wherein the cell selection is performed is by flow cytometry, fluorescence activated cell sorting, panning, affinity column separation, and/or magnetic selection.

39. (Amended) The method of claim 32, wherein steps (b) and (c) ~~the steps of contacting and selecting~~ comprise:
- (a b) ~~contacting a population of~~ the dissociated ~~cells containing a solid tumor stem cell~~ with a combination of reagents, wherein each reagent in the combination either selectively binds to either a solid tumor stem cell positive marker or negative marker and
  - (~~b~~ c) selecting cells that bind to reagents that selectively bind to the positive marker or that do not bind to reagents that selectively bind to the negative marker or a combination thereof, wherein the selected cells are enriched in tumor stem cells as compared with the population of unfractionated cells.
40. (Amended) The method of claim 32, further comprising the step of:
- (~~e~~ d) isolating the ~~proliferated~~ selected solid tumor stem cells.
41. (Canceled) The method of claim 32, further comprising the steps of:
- (d) introducing at least one selected cell to a culture medium that supports the growth of tumor stem cells; and
  - (e) proliferating the selected cell in the culture medium.
42. (Canceled) The method of claim 41, further comprising the step of:
- (f) introducing the proliferated cell into a host mammal.
43. (Canceled) The method of claim 41, further comprising the steps of:
- (f) contacting the proliferated cell with a test compound; and
  - (g) determining the effect of the test compound on the proliferated cell.
44. (Canceled) The method of claim 41, further comprising the steps of:
- (f) mixing a population of non-tumorigenic tumor cells with the solid tumor stem cells in culture, wherein the population of non-tumorigenic tumor cells
    - (i) is derived from a solid tumor;
    - (ii) is depleted for the ability to form tumors relative to unfractionated solid tumor cells; and
    - (iii) is depleted for cells that expresses the cell surface marker CD44 relative to unfractionated solid tumor cells.
45. (Canceled) The method of claim 44, further comprising the steps of :
- (g) transplanting the mixture into a host animal.

46.     (Canceled)            The method of claim 44, further comprising the steps of:  
         (g)            analyzing the mixture for an increase or decrease the ability of the solid tumor stem cells to survive or proliferate.
47.     (Canceled)            A method for stimulating an immune response to a solid tumor stem cell, comprising the steps of:  
         (a)            obtaining an enriched population of solid tumor stem cells; wherein  
                 (i)            the tumor cells are derived from a solid tumor;  
                 (ii)           the solid tumor stem cell expresses the cell surface marker CD44;  
                 (iii)          the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;  
                 (iv)          the solid tumor stem cell is tumorigenic; and  
                 (v)          the solid tumor stem cell population is enriched 2-fold relative to unfractionated tumor cells;  
         (b)            treating the population to prevent cell replication; and  
         (c)            administering the treated cell to a human or animal subject in an amount effective for inducing an immune response to solid tumor stem cells.
48.     (Canceled)            The method of claim 47, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
49.     (Canceled)            The method of claim 47, wherein the treatment kills the solid tumor stem cell.
50.     (Canceled)            The method of claim 47, wherein the administration is by injection or by oral administration.
51.     (Canceled)            The method of claim 47, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
52.     (Canceled)            The method of claim 47, wherein the solid tumor stem cell fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
53.     (Canceled)            The method of claim 47, further comprising the step of:  
         (d)            obtaining antibodies or antibody secreting hybridomas from the human or animal subject.
54.     (Canceled)            The method of claim 53, further comprising the step of:  
         (e)            testing the obtained antibody for the ability to specifically bind to solid tumor stem cells.
55.     (Canceled)            The method of claim 53, further comprising the step of:  
         (e)            testing the obtained antibody for the ability to bind to a polypeptide present on solid tumor stem cells.
56.     (Canceled)            The method of claim 53, further comprising the step of:  
         (e)            immunologically identifying a polypeptide present on solid tumor stem cells.

57. (Canceled) The method of claim 53, further comprising the step of:  
(e) immunologically identifying a polynucleotide encoding a polypeptide present on solid tumor stem cells.
58. (Canceled) The method of claim 53, further comprising the step of:  
(e) testing the obtained antibody for the ability to reduce tumor growth.
59. (Canceled) A method for stimulating an immune response to a solid tumor stem cell, comprising the steps of:  
(a) obtaining an enriched population of solid tumor stem cells; wherein  
(i) the tumor cells are derived from a solid tumor;  
(ii) the solid tumor stem cell expresses the cell surface marker CD44;  
(iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;  
(iv) the solid tumor stem cell is tumorigenic; and  
(v) the solid tumor stem cell population is enriched 2-fold relative to unfractionated tumor cells;  
(b) mixing the tumor stem cells in an *in vitro* culture with immune effector cells;  
(c) removing the immune effector cells from the culture; and  
(d) transplanting the immune effector cells into a host animal in a dose that is effective to stimulate an immune response in the animal.
60. (Canceled) The method of claim 59, wherein the solid tumor expresses the cell surface marker B38.1.
61. (Canceled) The method of claim 59, wherein the solid tumor fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
62. (Canceled) A purified population of polynucleotides, wherein the polynucleotides have been purified from an enriched population of solid tumor stem cells, wherein:  
(a) the tumor cells are derived from a solid tumor  
(b) the solid tumor stem cell expresses the cell surface marker CD44;  
(c) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;  
(d) the solid tumor stem cell is tumorigenic; and  
(e) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells.
63. (Canceled) The polynucleotide population of claim 63, wherein the solid tumor is a sarcoma or an epithelial cancer.
64. (Canceled) The polynucleotide population of claim 63, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
65. (Canceled) The polynucleotide population of claim 63, wherein solid tumor stem cell expresses the cell surface marker B38.1.



66.     (Canceled)        The polynucleotide population of claim 63, wherein the solid tumor fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
67.     (Canceled)        The polynucleotide population of claim 63, wherein the polynucleotides are affixed to a solid surface.
68.     (Canceled)        The polynucleotide population of claim 67, wherein the polynucleotides are affixed to the solid surface in an orderly array.
69.     (Canceled)        The polynucleotide population of claim 68, wherein the orderly array is a microarray.
70.     (Canceled)        The polynucleotide population of claim 63, wherein the polynucleotides are in a cDNA library.
71.     (Canceled)        The polynucleotide population of claim 63, wherein the polynucleotides have been amplified.
72.     (Canceled)        The polynucleotide population of claim 63, wherein the polynucleotides are labeled.
73.     (Canceled)        The polynucleotide population of claim 63, wherein the polynucleotides are used as a hybridization probe.
74.     (Canceled)        The polynucleotide population of claim 73, further comprising a microarray of polynucleotide sequences.
75.     (Canceled)        A purified population of polypeptides, wherein the polypeptides have been purified from an enriched population of solid tumor stem cells, wherein:
  - (a)     the tumor cells are derived from a solid tumor
  - (b)     the solid tumor stem cell expresses the cell surface marker CD44;
  - (c)     the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
  - (d)     the solid tumor stem cell is tumorigenic; and
  - (e)     the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells.
76.     (Canceled)        The polypeptide population of claim 75, wherein the solid tumor is a sarcoma or an epithelial cancer.
77.     (Canceled)        The polypeptide population of claim 75, wherein the solid tumor stem cells expresses the cell surface marker B38.1.
78.     (Canceled)        The polypeptide population of claim 75, wherein the solid tumor fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.

79. (Canceled) The polypeptide population of claim 75, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
80. (Canceled) The polypeptide population of claim 75, wherein the polypeptides are affixed to a solid surface.
81. (Canceled) The polypeptide population of claim 75, wherein the polypeptides are affixed to the solid surface in an orderly array.
82. (Canceled) The polypeptide population of claim 81, wherein the orderly array is a microarray.
83. (Canceled) The polypeptide population of claim 75, wherein the polypeptides are labeled.
84. (Canceled) The polypeptide population of claim 75, wherein the polypeptides are used as a probe.
85. (Canceled) The polypeptide population of claim 84, further comprising a microarray of components, wherein the components are selected from the group consisting of cells, polynucleotides, polypeptides, and test compounds.
86. (Canceled) A method for analyzing a population of cells enriched for solid tumor stem cells for gene expression patterns, comprising the steps of:
- (a) obtaining an population of cells enriched for solid tumor stem cells; wherein
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells; and
  - (b) analyzing the population of cells for gene expression patterns.
87. (Canceled) The method of claim 86, wherein the analysis is by a method selected from the group consisting of resequencing, high throughput screening, use of a microarray, use of analytical software for data collection and storage, use of analytical software for flexible formatting of data output, use of analytical software for statistical analysis of individual spot intensities to provide grouping and cluster analyses, and use of analytical software for linkage to external databases.
88. (Canceled) The method of claim 86, wherein the solid tumor is a sarcoma or an epithelial cancer.
89. (Canceled) The method of claim 86, wherein the solid tumor stem cell expresses the cell surface marker B38.1.

90. (Canceled) The method of claim 86, wherein the solid tumor stem cell fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
91. (Canceled) The method of claim 86, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
92. (Canceled) A method for analyzing a population of cells enriched for solid tumor stem cells for protein expression patterns, comprising the steps of:
- (a) obtaining an population of cells enriched for solid tumor stem cells; wherein
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells; and
  - (b) analyzing the population of cells for protein expression patterns.
93. (Canceled) The method of claim 92, wherein the analysis is by a method selected from the group consisting of mass spectrometry, high throughput screening, use of a microarray, use of analytical software for data collection and storage, use of analytical software for flexible formatting of data output, use of analytical software for statistical analysis of individual spot intensities to provide grouping and cluster analyses, and use of analytical software for linkage to external databases.
94. (Canceled) The method of claim 92, wherein the solid tumor is a sarcoma or an epithelial cancer.
95. (Canceled) The method of claim 92, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
96. (Canceled) The method of claim 92, wherein the solid tumor stem cell fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
97. (Canceled) The method of claim 92, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.

98. (Canceled) A method for determining the effect of a test compound on a solid tumor stem cell, comprising the steps of:
- (a) obtaining an enriched population of solid tumor stem cells, wherein:
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched 2-fold relative to unfractionated tumor cells;
  - (b) contacting the obtained cells with the test compound; and
  - (c) determining the response of the contacted cells to the test compound.
99. (Canceled) The method of claim 98, wherein the solid tumor is a sarcoma or an epithelial cancer.
100. (Canceled) The method of claim 98, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
101. (Canceled) The method of claim 98, wherein the solid tumor stem cell fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
102. (Canceled) The method of claim 98, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
103. (Canceled) The method of claim 98, wherein the solid tumor stem cells are localized in a manner selected from the group consisting of in monolayers in culture, in suspension in culture, and affixed to a solid surface.
104. (Canceled) The method of claim 98, wherein the contacting is effected at more than one concentration of the test compound being tested.
105. (Canceled) The method of claim 98, wherein the contacting is effected using microfluidic methods.
106. (Canceled) The method of claim 98, wherein the determination of the response of the contacted cells to the test compound comprises assaying for an effect selected from the group consisting of tumor formation, tumor growth, tumor stem cell proliferation, tumor cell survival, tumor cell cycle status, and tumor stem cell survival.
107. (Canceled) The method of claim 98, wherein the test compound is attached to a solid surface.
108. (Canceled) The method of claim 107, wherein the test compound is attached to a solid surface as a microarray.
109. (Canceled) The method of claim 98, wherein the test compound is in a set of other molecules.
110. (Canceled) The method of claim 98, wherein the test compound is in an array of other molecules.

111. (Canceled) The method of claim 98, further comprising the step of.  
(d) identifying the target in the contacted cells with which the test compound interacts.
112. (Canceled) A method for determining the effect of a test compound on a solid tumor stem cell, comprising the steps of:  
(a) obtaining an enriched population of solid tumor stem cells, wherein;  
(i) the tumor cells are derived from a solid tumor;  
(ii) the solid tumor stem cell expresses the cell surface marker CD44;  
(iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;  
(iv) the solid tumor stem cell is tumorigenic; and  
(v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells;  
(b) transplanting the obtained cells into an immunocompromised mouse;  
(c) administering a test compound to the immunocompromised mouse; and  
(d) determining the response of the transplanted solid tumor stem cells to the test compound.
113. (Canceled) The method of claim 112, wherein the solid tumor is a sarcoma or an epithelial cancer.
114. (Canceled) The method of claim 112, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
115. (Canceled) The method of claim 112, wherein the solid tumor stem cell fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
116. (Canceled) The method of claim 112, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.

117. (Canceled) A method for screening for a test compound that specifically binds to a solid tumor stem cell, comprising the steps of:
- (a) obtaining an enriched population of solid tumor stem cells, wherein:
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells;
  - (b) contacting the enriched population of solid tumor stem cells with a test compound under conditions suitable to allow complex formation; and
  - (c) detecting complex formation between the test compound and a solid tumor stem cell, wherein the presence of the complex identifies the test compound as specifically binding the tumor stem cell.
118. (Canceled) The method of claim 117, wherein the solid tumor is a sarcoma or an epithelial cancer.
119. (Canceled) The method of claim 117, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
120. (Canceled) The method of claim 117, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
121. (Canceled) The method of claim 117, wherein the solid tumor stem cell fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
122. (Canceled) A method for diagnosing the presence of solid tumor stem cells, comprising the steps of:
- (a) contacting the cells from a solid tumor with a reagent that binds to a positive marker for solid tumor stem cells; and
  - (b) detecting the contact between the reagent and the cells from the solid tumor, wherein an increased detection of the number of contacted cells as compared with the number of contacted cells in a benign tumor identifies the tumor as containing solid tumor stem cells.
123. (Canceled) The method of claim 122, wherein the detection is by flow-cytometry or immunohistochemistry.
124. (Canceled) The method of claim 122, wherein the solid tumor is a sarcoma or an epithelial cancer.
125. (Canceled) The method of claim 122, wherein the positive marker is a marker selected from the group consisting of CD44, B38.1 and ESA.

126. (Canceled) An *in vitro* method for the proliferation of a tumor stem cells, comprising the steps of:
- (a) obtaining an enriched population of solid tumor stem cells, wherein;
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched 2-fold relative to unfractionated tumor cells; and
  - (b) proliferating the obtained cells in a culture medium.
127. (Canceled) The method of claim 126, wherein the solid tumor is a sarcoma or an epithelial cancer.
128. (Canceled) The method of claim 126, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
129. (Canceled) The method of claim 126, wherein the solid tumor stem cell fails to express a marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
130. (Canceled) The method of claim 126, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
131. (Canceled) An *in vivo* method for the proliferation of a tumor stem cells, comprising the steps of:
- (a) obtaining an enriched population of solid tumor stem cells, wherein;
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells; and
  - (b) transplanting the isolated cell into a host mammal under conditions that allow the proliferation of solid tumor stem cells in the host mammal.
132. (Canceled) The method of claim 131, wherein the solid tumor is a sarcoma or an epithelial cancer.
133. (Canceled) The method of claim 131, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
134. (Canceled) The method of claim 131, wherein the solid tumor stem cell fails to express a marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.

135. (Canceled) The method of claim 131, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
136. (Canceled) The method of claim 131, further comprising the step of:  
(c) isolating the proliferated tumor cells from the host mammal.
137. (Canceled) A method for producing genetically modified tumor stem cells, comprising the steps of:  
(a) obtaining an enriched population of solid tumor stem cells, wherein;  
(i) the tumor cells are derived from a solid tumor;  
(ii) the solid tumor stem cell expresses the cell surface marker CD44;  
(iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;  
(iv) the solid tumor stem cell is tumorigenic; and  
(v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells; and  
(b) genetically modifying the obtained cells.
138. (Canceled) The method of claim 137, wherein the solid tumor is a sarcoma or an epithelial cancer.
139. (Canceled) The method of claim 137, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
140. (Canceled) The method of claim 137, wherein the solid tumor stem cell fails to express a marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
141. (Canceled) The method of claim 137, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
142. (Canceled) The method of claim 137, in which the genetic modification is performed *in vitro*.
143. (Canceled) The method of claim 142, in which the genetic modification is performed *in vivo*.
144. (Canceled) The method of claim 137, wherein the genetic modification is the introduction of a plasmid into the solid tumor stem cell.
145. (Canceled) The method of claim 137, wherein the genetic modification is the introduction of a viral vector into the solid tumor stem cell.
146. (Canceled) The method of claim 137, in which the virus has been modified to express a protein that recognizes an antigen on the solid tumor stem cell, thus specifically targeting the virus to solid tumor stem cell.



147. (Canceled) The method of claim 137, further comprising the step of:  
(c) examining the effect of the genetic modification on tumor formation, tumor growth, tumor cell proliferation, tumor cell survival, tumor stem cell survival, tumor stem cell proliferation, tumor cell cycle status, and tumor stem cell frequency.
148. (Canceled) An *in vivo* method for proliferating a population of cancer cells, comprising:  
(a) introducing an enriched population of solid tumor stem cells into an immunocompromised mouse; wherein;  
(i) the tumor cells are derived from a solid tumor;  
(ii) the solid tumor stem cell expresses the cell surface marker CD44;  
(iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;  
(iv) the solid tumor stem cell is tumorigenic; and  
(v) the solid tumor stem cell population is enriched 2-fold relative to unfractionated tumor cells; and  
(b) proliferating the solid tumor stem cells in the mouse; and  
(c) purifying the proliferated solid tumor stem cells from the mouse.
149. (Canceled) The method of claim 148, wherein the solid tumor is a sarcoma or an epithelial cancer.
150. (Canceled) The method of claim 148, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
151. (Canceled) The method of claim 148, wherein the solid tumor stem cell fails to express a marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
152. (Canceled) The method of claim 148, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
153. (Canceled) The method of claim 148, wherein the mouse is a NOD/SCID mouse or a SCID/Beige mouse.
154. (Canceled) The method of claim 148, wherein the cells are introduced subcutaneously or into the mammary fat pad.
155. (Canceled) The method of claim 148, wherein tumors grow in the mammal in greater than 75% of the introductions.
156. (Canceled) The method of claim 148, wherein tumors grow in the mammal in greater than 90% of the introductions.
157. (Canceled) The method of claim 148, wherein the population of cells has been enriched at least 2-fold.
158. (Canceled) The method of claim 148, wherein the population of cells has been enriched at least 5-fold.

159. (Canceled) The method of claim 148, wherein the population of cells has been enriched at least 10-fold.
160. (Canceled) The method of claim 148, wherein the mice have been further immunosuppressed by a method selected from the group consisting of administration of VP16, radiation therapy and chemotherapy.
161. (Canceled) The method of claim 148, further comprising:  
(d) isolating an enriched population of solid tumor stem cells from the proliferated cells
162. (Canceled) The method of claim 161, wherein the isolation comprises the use of flow-cytometry.
163. (Canceled) A method for growing a solid tumor stem cell from a solid tumor, comprising the steps of  
(a) separating the cells of the solid tumor;  
(b) suspending the separated tumor cells in suspension; and  
(c) introducing the suspended cell into a host mammal, such that the cancer stem cell in the introduced suspension forms a tumor in the host mammal.
164. (Canceled) The method of claim 163, wherein the solid tumor is a sarcoma or an epithelial cancer.
165. (Canceled) The method of claim 163, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
166. (Canceled) The method of claim 163, wherein the solid tumor stem cell fails to express a marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
167. (Canceled) A tumor bank, comprising cells derived from a single tumor, wherein the tumor has been produced by the steps of:  
(a) introducing an enriched population of tumor stem cells into a host mammal; wherein  
(i) the tumor cells are derived from a solid tumor;  
(ii) the solid tumor stem cell expresses the cell surface marker CD44;  
(iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;  
(iv) the solid tumor stem cell is tumorigenic; and  
(v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells;  
(b) proliferating the introduced cells in the host mammal; and  
(c) isolating the proliferated cells from the host mammal.
168. (Canceled) The tumor bank of claim 167, wherein the solid tumor is a sarcoma or an epithelial cancer.

169. (Canceled) The tumor bank of claim 167, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
170. (Canceled) The tumor bank of claim 167, wherein the solid tumor stem cell fails to express a marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
171. (Canceled) The tumor bank of claim 167, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
172. (Canceled) A chimeric mammal, comprising:
- (a) the mammal; and
  - (b) an enriched population of solid tumor stem cells, wherein
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells; and
    - (vi) the cells of the enriched population have been injected into the mammal.
173. (Canceled) The chimeric mammal of claim 172, wherein the solid tumor of (b)(iv) is a sarcoma or an epithelial cancer.
174. (Canceled) The chimeric mammal of claim 172, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
175. (Canceled) The chimeric mammal of claim 172, wherein the solid tumor stem cell fails to express at least one lineage marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
176. (Canceled) The chimeric mammal of claim 172, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
177. (Canceled) The chimeric mammal of claim 172, wherein the mammal is an immunocompromised mouse.

178. (Canceled) An *in vivo* method for modeling a tumor treatment regime, comprising the steps of:
- (a) introducing an enriched population of solid tumor stem cells into an immunocompromised mouse under conditions that allow the solid tumor stem cells to proliferate to form a tumor; wherein
    - (i) the tumor cells are derived from a solid tumor;
    - (ii) the solid tumor stem cell expresses the cell surface marker CD44;
    - (iii) the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor;
    - (iv) the solid tumor stem cell is tumorigenic; and
    - (v) the solid tumor stem cell population is enriched at least 2-fold relative to unfractionated tumor cells; and
  - (b) testing the effects of treatment regimens on the solid tumor cells in the immunocompromised mouse by monitoring the effect of the treatment regimen.
179. (Canceled) The method of claim 178, wherein the solid tumor is a sarcoma or an epithelial cancer.
180. (Canceled) The method of claim 178, wherein the solid tumor stem cell expresses the cell surface marker B38.1.
181. (Canceled) The method of claim 178, wherein the solid tumor stem cell fails to express a marker selected from the group consisting of CD2, CD3, CD14, CD16, CD45 and CD64.
182. (Canceled) The method of claim 178, wherein the enriched population of solid tumor stem cells is an isolated solid tumor stem cell.
183. (Canceled) A method for reducing the size of a solid tumor, comprising  
contacting the cells of the solid tumor with a therapeutically effective amount of an antibody directed against a Notch protein.
184. (Canceled) The method of claim 183, wherein the antibody is directed against a Notch 4 polypeptide.
185. (Canceled) The method of claim 184, wherein the antibody is directed against the extracellular domain of Notch 4.
184. (New) The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell expresses at least one marker selected from the group consisting of CD44, epithelial specific antigen (ESA), and B38.1.
185. (New) The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell expresses the cell surface marker B38.1.

186. (New) The isolated solid tumor stem cell of claim 1, wherein the solid tumor stem cell expresses lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor.
187. (New) The isolated solid tumor stem cell of claim 8, wherein the LINEAGE markers further comprise CD10, CD31, and CD140b.
188. (New) The method of claim 33, wherein the epithelial cancer is a breast cancer or an ovarian cancer.
189. (New) The isolated solid tumor stem cell of claim 15, wherein the animal is an immunocompromised animal.
190. (New) The isolated solid tumor stem cell of claim 15, wherein the animal is a mammal.
191. (New) The isolated solid tumor stem cell of claim 190, wherein the mammal is an immunocompromised mammal.
192. (New) The isolated solid tumor stem cell of claim 190, wherein the mammal is a mouse.
193. (New) The isolated solid tumor stem cell of claim 17, wherein the immunocompromised mouse is selected from the group consisting of nude mouse, SCID mouse, NOD/SCID mouse, Beige/SCID mouse; and  $\beta$ 2 microglobulin deficient NOD/SCID mouse.
194. (New) The enriched population of claim 24, wherein the epithelial cancer is a breast cancer or an ovarian cancer.

195. (New) The enriched population of claim 23, wherein the solid tumor stem cells in the enriched population express at least one marker selected from the group consisting of CD44, epithelial specific antigen (ESA), and B38.1.
196. (New) The enriched population of claim 23, wherein the solid tumor stem cells in the enriched population express the cell surface marker B38.1.
197. (New) The enriched population of claim 23, wherein the solid tumor stem cells in the enriched population express lower levels of the marker CD24 than the mean expression of CD24 by non-tumorigenic cancer cells derived from the solid tumor.
198. (New) The method of claim 33, wherein the epithelial cancer is a breast cancer or an ovarian cancer.